

Remarks

In the Office Action mailed May 7, 2004, claims 21-41 were withdrawn from consideration by the Examiner. Claim 1 has been canceled, claims 2, 5, 9-11, and 15-19 have been amended and claims 42 and 43 have been added by Applicant in this amendment. Applicant acknowledges the Examiner's withdraw of the § 102(a) and § 102(b) rejections, and the § 103(a) rejection based on Schoonjans *et al.*, in view of Leung *et al.*, and Lindhofer *et al.* The Examiner presently rejects claims 5, 7, and 8 under 35 U.S.C. § 112, first paragraph, for lack of enablement, and claims 1-12 and 15-20 under 35 U.S.C. § 103(a) as being unpatentable over Schoonjans *et al.*, in view of Hansen *et al.*, and Lindhofer *et al.*, and claims 1-2, 9-10, and 15-20 under 35 U.S.C. § 103(a) as being unpatentable over Schoonjans *et al.*, in view of Hansen *et al.*, and Lindhofer *et al.*. The specific grounds for objection, and Applicant's response thereto, are set out in detail below.

Claims 2-12, 15-20, 42 and 43 are presently under consideration. Support for newly added claim 42 can be found in canceled claim 1 and in the specification at page 33 (first paragraph) to page 34 (first paragraph). Support for newly added claim 43 can be found in canceled claim 1 and in the specification at page 33 (first paragraph) to page 34 (first paragraph), page 33 (last paragraph) and Example 1.

Rejection under § 112, first paragraph

Claims 5, 7 and 8 are rejected under 35 U.S.C. § 112, first paragraph, because the specification allegedly does not enable "derivatives of" an immunoglobulin light chain variable or constant region domain or "derivatives of" an immunoglobulin heavy chain variable or constant region domain. Applicant respectfully traverses.

Applicant submits that one skilled in the art would readily be able to readily determine and generate the full scope of the target binding proteins encompassed by claims 5, 7 and 8 by employing no more than routine experimentation. In particular, the term "derivative" is clearly defined at page 10, lines 10-19 of the specification. Nevertheless, without acquiescing in the propriety of the rejection, Applicant has amended claim 5 to remove the recitation of "or a derivative thereof", thereby mooting the rejection. Accordingly, withdrawal of the rejection respectfully is requested.

Rejection under § 103(a)

Claims 1-12 and 15-20 are rejected by the Examiner under 35 U.S.C. § 103 as being obvious over Schoonjans *et al.* (WO 99/37791), in view of Hansen *et al.* (US 5,635,603) and Lindhofer *et al.* (U.S. Publication No. 20002/0051780). Claims 1-2, 9-10, and 11-18 are rejected as obvious over Harris *et al.* (WO 94/09131), in view of Chaudhary *et al.* (PNAS 87:1066-70, 1990) and Hansen *et al.* (U.S. Patent No. 6,254,868).

Schoonjans *et al.*, in view of Hansen *et al.* and Lindhofer *et al.*

The Examiner admits that Schoonjans *et al.* does not teach an N-glycosylation site, a toxin linked to the carbohydrate site, the linkers of SEQ ID NOS:1 and 2, or molecules that bind to CD28 and CD3, but asserts that these deficiencies are made up for by the teachings of Hansen *et al.* and Lindhofer *et al.* Applicant respectfully traverse.

All claims are presumed initially to be non-obvious. A *prima facie* case of obviousness requires three elements: (1) a teaching or suggestion of all of the claim limitations; (2) a suggestion or motivation to modify or combine the teachings of the applied prior art; and (3) a reasonable expectation of success in reaching the claimed invention. The Examiner bears the initial burden of supporting any *prima facie* assertion of obviousness with adequate facts. MPEP § 2142 (Feb. 2000).

Here, none of the cited references, either alone or in combination, disclose all the elements of claim 42 or claim 43. Accordingly, the first element of a *prima facie* case of obviousness cannot be satisfied and withdrawal of the rejection respectfully is requested.

Specifically, claim 1 has been canceled and claim 42 is directed to a target binding protein "wherein at least one of said Fab or Fab' heavy or light chains comprises a constant region N-glycosylation recognition sequence; and wherein a carbohydrate chain is linked to said N-glycosylation recognition sequence." [emphasis added]. Claim 43 further specifies that at least one of the binding sites is selected from the Fv of mAb hMN14, and at least one of the binding sites is selected from the Fv of mAb 734. Schoonjans not only fails to teach or suggest molecules that contain a constant region N-glycosylation recognition sequence as required by claim 42, but also fails to teach molecules having the specificities recited in claim 43.

Hansen *et al.* is directed to immunoconjugates of a conventional light chain/heavy chain antibody or antibody fragment containing a glycosylation site at a specific position in the variable

domain of the antibody light chain. There is no teaching or suggestion in Hansen *et al.* that introduction of a glycosylation site anywhere else other than at the defined position of the light chain variable domain would be useful or desirable.

Lindhoffer *et al.* is cited as teaching bispecific or trispecific antibodies that bind to tumour-associated antigens, CD3 and CD28 but fails to cure the deficiencies of Schoonjans *et al.* and Hansen *et al.* Therefore, claims 1-12 and 15-20, as well as newly presented claims 42 and 43, are not obvious over Schoonjans *et al.* in view of Hansen *et al.* and Lindhofer *et al.*

In sum, the Examiner has failed to set forth a *prima facie* case of obviousness and withdrawal of the rejection respectfully is requested.

Harris *et al.*, in view of Chaudhary *et al.* and Hansen *et al.*

Claims 1-2, 9-10, and 11-18 are rejected as obvious over Harris *et al.* (WO 94/09131), in view of Chaudhary *et al.* (PNAS 87:1066-70, 1990) and Hansen *et al.* (U.S. Patent No. 6,254,868). Harris *et al.* allegedly describes an Fv where each chain of the Fv is linked to an scFv molecule, although the Examiner admits that Harris *et al.* fails to teach or describe either a conjugate at the C-terminal of the polypeptide, or a glycosylation site for conjugations to toxins, or binding to toxin and tumor antigens. These deficiencies are, however, allegedly made up for in the teachings of Chaudhary *et al.* and Hansen *et al.* Applicant respectfully traverses.

The molecules allegedly described by Harris *et al.* do not contain a Fab or Fab' as required by the instant claims and, by definition, cannot contain a constant region N-glycosylation recognition sequence. This deficiency is not cured by either of the secondary references.

As discussed above, Hansen *et al.* is directed to immunoconjugates comprising an antibody or antibody fragment containing a glycosylation site in the variable domain of the antibody light chain. There is no teaching or suggestion in Hansen *et al.* that introduction of a glycosylation site anywhere else other than at the defined position of the light chain variable domain would be useful or desirable. Chaudhary *et al.* merely is directed to a method for rapidly cloning the functional variable region sequences of many different antibodies from hybridoma RNA.

The teachings of Chaudhary *et al.* and Hansen *et al.* therefore do not cure the deficiencies of Harris *et al.* The cited combination of references fails to either teach or suggest all of the elements recited in the instantly pending claims. Accordingly, the Examiner has failed to set forth a *prima facie* case of obviousness over Harris *et al.* in view of Chaudhary *et al.* and Hansen *et al.* and the rejection should be withdrawn.

CONCLUSION

In view of the above remarks and amendments, it is respectfully submitted that this application is in condition for allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to telephone the undersigned at the number listed below if the Examiner believes such would be helpful in advancing the application to issue.

If any additional fees are required for the filing of this paper, Applicant authorizes the Commissioner to charge any deficiency to Deposit Account No. 08-1641.

Respectfully submitted,

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